REMARKS

After entry of this amendment, claims 1-8, 10-13, and 22-23 are pending. Claims 14-21 have been canceled without prejudice to future prosecution.

Claim rejections under 35 U.S.C. § 103(a)

Claims 1-8, 10-13, and 22-23 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,124,110 to Wober *et al.*; U.S. Patent No. 5,625,036 to Hawkins *et al.*; Lawson *et al.*, *J. Biol. Chem.* 267(7): 4834-4843 (1992); Varadi *et al.*, *J. Thromb. Haemostasis* 1:2374-2380 (2003); U.S. Patent No. 5,952,198 to Chan; U.S. Patent No. 6,074,826 to Hogan *et al.*; U.S. Patent No. 6,576,422 to Weinstein *et al.*; U.S. Patent No. 6,756,019 to Dubrow *et al.*, U.S. Patent Publication No. 2002/0151582 to Dou *et al*; and p. B-77 of the CRC Handbook of Chemistry and Physics 51st ed., R.C. Weast, ed. Applicants respectfully traverse.

The Patent Office bears the burden of establishing a prima facie case of obviousness under 35 U.S.C. § 103. As set forth in M.P.E.P. § 2141 (I), the Patent Office's policy is to follow *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966), in the consideration and determination of obviousness under 35 U.S.C. § 103. The four factual inquires enunciated in *Graham* for determining obviousness are as follows:

(A) Determining the scope and content of the prior art;

(B) Ascertaining the differences between the prior art and the claimed invention;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations.

Moreover, the claimed invention must be considered as a whole and an assessment as to whether there is a reasonable expectation of success in combining the references.

To support a rejection under 35 U.S.C. § 103 using the Federal Circuit's teaching-suggestion-motivation (TSM) test, the Patent Office must provide evidence that demonstrates some suggestion or motivation to modify or combine the references, whether in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*,

837 F.2d 1071, 1074 (Fed. Cir. 1988); M.P.E.P. § 2143. Next, the Office must show that one of ordinary skill in the art would have had a reasonable expectation of success in modifying the prior art references, or in combining their relevant teachings. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). Finally, the Office must show that the combined prior art references "teach or suggest all the claim[ed] limitations." M.P.E.P. § 2143.

Applicants respectfully resubmit that the combination of cited references does not render the presently claimed invention obvious for at least the following reason: the combination of references does not teach or suggest "a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label, wherein the lyophilized mixture forms a clear solution when dissolved in an aqueous solution."

The present invention is directed to a kit comprising the following components and attributes as claimed: (1) a lyophilized tissue factor (TF)/phospholipid (PL)-complex; and (2) a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label. Addition of an aqueous solution to the lyophilized mixture leads to formation of a clear, precipitate-free solution. As explained by Dr. Turecek in his Declaration under 37 C.F.R 1.132, it is a discovery of the invention that it is possible to produce a lyophilized mixture of $CaCl_2$ and a fluorescent thrombin substrate which forms a clear solution when dissolved in an aqueous solution. Prior to the invention, one of skill in the art would have expected that the mixture of the fluorescent thrombin substrate and $CaCl_2$ would lead to the formation of a precipitate.

Failure to teach or suggest all the claim limitations

Applicants reassert that the presently claimed invention is not obvious in view of the cited art for at least the following reason: the combination of references does not teach or suggest "a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label, wherein the lyophilized mixture forms a clear solution when dissolved in an aqueous solution". There is no hint or suggestion in any of the references that the substrates are lyophilized as a mixture with $CaCl_2$.(*see*, Declaration ¶ 8).

Wober *et al.* discloses methods of measuring thrombin generation using dried chromogenic substrates, but does not disclose or suggest use of a fluorescent substrate for measuring thrombin generation, much less a lyophilized mixture comprising $CaCl_2$ and the thrombin substrate. Hawkins *et al.* describes a prothrombin reagent (PT) containing recombinant tissue factor, natural or synthetic phospholipids, calcium ion, and a buffer (*see*, col. 2, line 66 to col. 3, line 1). Hawkins indicates that tissue factor-containing reagents should be stable in a lyophilized state (*see*, col. 1, lines 43-50), but does not disclose or suggest anything regarding nature of the substrates for a thrombin generation assay. Lawson *et al.* discloses methods of measuring Factor VIIa activity using dried fluorescent substrates, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. Varadi *et al.*, discloses methods of measuring thrombin generation using dried fluorescent substrates, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate or using such a mixture in the methods. All of the aforementioned references are completely devoid of any disclosure or suggestion of a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. Dou *et al.* disclose methods using fluorescent substrates. to detect the inhibition of proteasome activity by tea polyphenols (*see*, col. 5, paragraph 56), but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. CRC discloses that $CaCl_2$ is soluble in an aqueous solution, *i.e.*, water, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate.

Moreover, as Dr. Turecek's explains in ¶ 9 of his declaration, at least four of the cited references are not even relevant to detection of any protein activity, much less thrombin activity: Chan; Hogan *et al.*; Weinstein *et al.*; and Dubrow *et al.* Chan discloses culturing mammalian cells in the presence of a liposome-like substance to increase recombinant Factor VIII production (*see*, abstract); Hogan *et al.* discloses methods and kits for detecting *Borrelia* nucleic acids and indicates that enzymes, nucleotide triphosphates, primers and probes may be lyophilized (*see*, col. 37, lines 15-17); Weinstein *et al.* discloses methods of detecting using reporter genes to detect a target of interest (col. 1, line 66 to col. 2, line 17). The methods of

Weinstein *et al.* may employ a lyophilized "cell or viral detector composition" (*i.e.*, reporter gene) immobilized on a solid support (*see*, col. 16, lines 4-11), but do not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. Dubrow *et al.* describes multifluidic devices which may contain a reagent immobilized onto a semi-permeable membrane using lyophilization (col 13, lines 5-6).

Because the combination of references does not disclose or suggest a lyophilized mixture of a fluorescent substrate and $CaCl_2$ that forms a clear solution when dissolved in aqueous solution, the combination does not teach or suggest every element of the present claims. For this reason alone, a *prima facie* case of obviousness has not been made by the Examiner.

No reasonable expectation of success

Moreover, the skilled artisan would have no reasonable expectation of success by combining the references as suggested by the Examiner. As explained in detail in the instant specification and by Dr. Turecek in his Declaration, the addition of $CaCl_2$ to a fluorescent substrate in aqueous solution leads to formation of a precipitate. Accordingly, without the teachings of the instant specification, the skilled artisan would expect that lyophilization of a fluorescent substrate in the presence of $CaCl_2$ would result in a precipitate when such a lyophilized powder is reconstituted with an aqueous buffer or water, not the clear solution as presently claimed.

Dr. Turecek explains that the specification sets forth experiments demonstrating that the addition of $CaCl_2$ to a fluorescent substrate in solution leads to formation of a precipitate (*see, e.g.,* page 9, paragraph 28 to page 10, paragraph 29). The precipitate was dissolved only after vigorous shaking of the solution at 37°C, followed by slow stirring at room temperature for at least an hour (*see*, *e.g.*, page 10, paragraph 50) (*see*, Declaration ¶ 10).

Dr. Turecek presents the results of two separate sets of additional experiments that demonstrate that the addition of $CaCl_2$ to a fluorescent substrate in solution leads to formation of a precipitate that can be dissolved only after extensive warming and stirring (*see*, Declaration ¶ 11). In the first set of additional experiments, small amounts (25 mg) of the

fluorescent substrate Z-Gly-GLy-Arg-AMC.HCl in powder form were dissolved in 10% DMSO-Hna (*i.e.*, an organic solution containing 10% DMSO; 25 nM Hepes, and 175 nM NaCl, pH 7.35). A solution of 1M $CaCl_2$ was added to the dissolved substrate. Formation of a white, cloudy precipitate was immediately observed. Absorbance measurements taken before and thirty minutes after the addition of the $CaCl_2$ are set forth in Table 1 below and demonstrate that the mixture of the $CaCl_2$ and the fluorescent thrombin substrate is not a clear solution.

Sample	**OD_{405}* prior to addition of $CaCl_2$**	**OD_{405}* 30 minutes following addition of $CaCl_2$**
1	0.0435	0.0485
2	0.0435	0.2155
3	0.0445	0.2975

* OD_{405} is average of two wells

In the second set of additional experiments, full vials (250 mg) of the fluorescent substrate Z-Gly-GLy-Arg-AMC.HCl in powder form were dissolved in 0% DMSO-Hna (panel 1 of Exhibit B). Again, formation of a white, cloudy precipitate was immediately observed (panel 2 of Exhibit B). The precipitate could only be dissolved upon warming the solution for 15 minutes at 37 °C, followed by stirring at room temperature for at least 45 minutes (panel 3 of Exhibit B). After the solution was stored at room temperature for 30-120 minutes (required for aliquoting), the solution became opalescent and a stable precipitate formed (panels 4 and 7 of Exhibit B). Again, the precipitate dissolved only after extensive and vigorous mixing (panels 5-6 and 8-9 of Exhibit B).

Thus, without the teachings of the instant specification, one of skill in the art would have had no reasonable expectation that lyophilization of a fluorescent substrate in the presence of $CaCl_2$ would result in the clear solution upon reconstitution in an aqueous solution.

In view of the foregoing remarks, Applicants submit that a *prima facie* case of obviousness has not been established and the presently claimed invention is nonobvious and thus

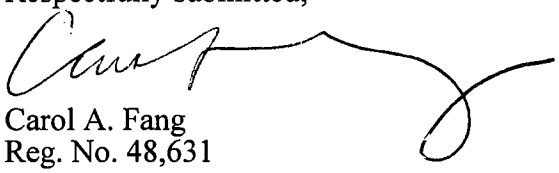
patentable over the cited references. Accordingly, Applicants request withdrawal of the rejection under 35 U.S.C. §103.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 925-472-5000.

Respectfully submitted,



Carol A. Fang
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CAF
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EXHIBIT A

PATENT
Attorney Docket No.: 20695C-008700US
Client Reference No. PL-279.00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No. 9454
Varadi *et al.*	Examiner: Rosanne Kosson
Application No.: 10/816,099	Technology Center/Art Unit: 1653
Filed: March 31, 2004	DECLARATION OF DR. PETER TURECEK UNDER 37 C.F.R. § 1.132
For: KITS FOR MEASURING THROMBIN GENERATION	
Customer No.: 44183	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

1. I, Peter Turecek, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both (18 U.S.C. § 1001), and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

2. All statements herein made of my own knowledge are true, and statements made on information or belief are believed to be true and correct.

3. I received my Magister pharmaciae from the University of Vienna in 1985 and my Ph.D. from the University of Vienna in 1987. I am currently the Senior Director of Preclinical Research & Development of the Baxter BioScience Division of Baxter Healthcare, Baxter AG, Vienna. I have been in this position since 2005. I have been in this and related positions since 1989. I have numerous scientific publications in the field of biochemical and analytical diagnostics. A copy of my CV is attached as Exhibit A.

4. I am a named inventor on the above-referenced patent application. I have read and am familiar with the contents of the subject patent application. I have also read the Office Action received from the United States Patent and Trademark Office dated August 28, 2006 and the references cited therein, *i.e.*, U.S. Patent No. 6,124,110 to Wober *et al.*; U.S. Patent No. 5,625,036 to Hawkins *et al.*; Lawson *et al.*, *J. Biol. Chem.* 267(7): 4834-4843 (1992); Varadi *et al.*, *J. Thromb. Haemostasis* 1:2374-2380 (2003); U.S. Patent No. 5,952,198 to Chan; U.S. Patent No. 6,074,826 to Hogan *et al.*; U.S. Patent No. 6,576,422 to Weinstein *et al.*; U.S. Patent No. 6,756,019 to Dubrow *et al.*, U.S. Patent Publication No. 2002/0151582 to Dou *et al*; and p. B-77 of the CRC Handbook of Chemistry and Physics 51st ed., R.C. Weast, ed.. It is my understanding that the Examiner is acknowledging that the combination of cited references does not disclose all of the elements of the presently claimed invention, but is alleging that the combination of references suggests a lyophilized preparation comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label that forms a clear solution when dissolved in an aqueous solution.

5. The present invention relates to kits for measuring thrombin generation. The kits comprise (i) a lyophilized tissue factor (TF)/phospholipid (PL)-complex; and (ii) a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label, wherein the lyophilized mixture forms a *clear* solution when dissolved in an aqueous solution. This declaration is presented to clarify that (1) the combination of references does not disclose or suggest the lyophilized mixture; and (2) one of skill in the art would have no reasonable expectation of success in arriving at the claimed invention based on the combination of references.

6. The claimed kits comprise a lyophilized mixture comprising $CaCl_2$ and thrombin substrate comprising a fluorescent label. It is a discovery of the invention that it is possible to produce a lyophilized mixture of $CaCl_2$ and a fluorescent thrombin substrate which forms a clear solution when dissolved in an aqueous solution. Prior to our invention, one of skill in the art would have expected that the mixture of the fluorescent thrombin substrate and $CaCl_2$ would lead to the formation of a precipitate.

7. This declaration presents results from experiments demonstrating that the addition of $CaCl_2$ to a fluorescent substrate in an aqueous solution leads to formation of a precipitate that can be dissolved only following continuous agitation (*i.e.*, stirring and shaking). All of the experiments described herein were conducted under my supervision as Senior Director Research & Development, and are described in detail below.

None of the references disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label, wherein the lyophilized mixture forms a clear solution when dissolved in an aqueous solution.

8. Wober *et al.* discloses methods of measuring thrombin generation using dried chromogenic substrates, but does not disclose or suggest use of a fluorescent substrate for measuring thrombin generation, much less a lyophilized mixture comprising $CaCl_2$ and the thrombin substrate. Hawkins *et al.* describes a prothrombin reagent (PT) containing recombinant tissue factor, natural or synthetic phospholipids, calcium ion, and a buffer (*see*, col. 2, line 66 to col. 3, line 1). Hawkins indicates that tissue factor-containing reagents should be stable in a lyophilized state (*see*, col. 1, lines 43-50), but does not disclose or suggest anything regarding nature of the substrates for a thrombin generation assay. Lawson *et al.* discloses methods of measuring Factor VIIa activity using dried fluorescent substrates, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. Varadi *et al.*, which is my own work, discloses methods of measuring thrombin generation using dried fluorescent substrates, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate or using such a mixture in the methods. All of the aforementioned references are completely devoid of any disclosure or suggestion of a lyophilized mixture comprising $CaCl_2$ and a flourescent thrombin substrate. Dou *et al.* disclose methods using fluorescent substrates. to detect the inhibition of proteasome activity by tea polyphenols (*see*, col. 5, paragraph 56), but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. CRC discloses that $CaCl_2$ is soluble in an aqueous solution, *i.e.*, water, but does not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate.

9. Moreover, at least four of the cited references are not even relevant to detection of any protein activity, much less thrombin activity; Chan; Hogan *et al.*; Weinstein *et al.*; and Dubrow *et al.*. Chan discloses culturing mammalian cells in the presence of a liposome-like substance to increase recombinant Factor VIII production (*see*, abstract); Hogan *et al.* discloses methods and kits for detecting *Borrelia* nucleic acids and indicates that enzymes, nucleotide triphosphates, primers and probes may be lyophilized (*see*, col. 37, lines 15-17); Weinstein *et al.* discloses methods of detecting using reporter genes to detect a target of interest (col. 1, line 66 to col. 2, line 17). The methods of Weinstein *et al.* may employ a lyophilized "cell or viral detector composition" (*i.e.*, reporter gene) immobilized on a solid support (*see*, col. 16, lines 4-11), but do not disclose or suggest a lyophilized mixture comprising $CaCl_2$ and a fluorescent thrombin substrate. Dubrow *et al.* describes multifluidic devices which may contain a reagent immobilized onto a semi-permeable membrane using lyophilization (col 13, lines 5-6).

One of skill in the art would not have expected that the combination of references would lead to a lyophilized mixture of $CaCl_2$ and a fluorescent thrombin substrate which forms a clear solution when dissolved in an aqueous solution.

10. First, as set forth in the specification, the addition of $CaCl_2$ to a fluorescent substrate in solution leads to formation of a precipitate (*see, e.g.*, page 9, paragraph 28 to page 10, paragraph 29). The precipitate was dissolved only after vigorous shaking of the solution at 37°C, followed by slow stirring at room temperature for at least an hour (*see, e.g.*, page 10, paragraph 50).

11. Second, two separate sets of additional experiments demonstrate that the addition of $CaCl_2$ to a fluorescent substrate in solution leads to formation of a precipitate that can be dissolved only after extensive warming and stirring. In the first set of additional experiments, small amounts (25 mg) of the fluorescent substrate Z-Gly-GLy-Arg-AMC.HCl in powder form were dissolved in 10% DMSO-Hna (*i.e.*, an organic solution containing 10% DMSO; 25 nM Hepes, and 175 nM NaCl, pH 7.35). A solution of 1M $CaCl_2$ was added to the dissolved substrate. Formation of a white, cloudy precipitate was immediately observed. Absorbance measurements taken before and thirty minutes after the addition of the $CaCl_2$ are set forth in

Table 1 below and demonstrate that the mixture of the $CaCl_2$ and the fluorescent thrombin substrate is not a clear solution.

Sample	OD_{405}* prior to addition of $CaCl_2$	OD_{405}* 30 minutes following addition of $CaCl_2$
1	0.0435	0.0485
2	0.0435	0.2155
3	0.0445	0.2975

* OD_{405} is average of two wells

12. In the second set of additional experiments, full vials (250 mg) of the fluorescent substrate Z-Gly-GLy-Arg-AMC.HCl in powder form were dissolved in 0% DMSO-Hna (panel 1 of Exhibit B). Again, formation of a white, cloudy precipitate was immediately observed (panel 2 of Exhibit B). The precipitate could only be dissolved upon warming the solution for 15 minutes at 37 °C, followed by stirring at room temperature for at least 45 minutes (panel 3 of Exhibit B). After the solution was stored at room temperature for 30-120 minutes (required for aliquoting), the solution became opalescent and a stable precipitate formed (panels 4 and 7 of Exhibit B). Again, the precipitate dissolved only after extensive and vigourous mixing for up to 15 minutes (panels 5-6 and 8-9 of Exhibit B).

13. The data set forth above unequivocally demonstrate that addition of $CaCl_2$ to the fluorescent thrombin substrate solution leads to formation of a precipitate that can only be dissolved by extensive warming and stirring. Thus, without the disclosure of the specification, one of skill in the art would not have expected that a lyophilized mixture of comprising $CaCl_2$ and fluorescent thrombin substrate would form a clear solution when dissolved in an aqueous solution.

14. In view of the foregoing, it is my scientific opinion that the combination of Wober *et al.*, Hawkins *et al.*, Lawson *et al.*, Varadi *et al.*, Chan, Hogan *et al.*, Weinstein *et al.*, Dubrow *et al.*, and Dou *et al.* does not suggest all of the elements of the claimed kits for measuring thrombin generation, in particular, a lyophilized mixture comprising $CaCl_2$ and a thrombin substrate comprising a fluorescent label that forms a clear solution when dissolved in

an aqueous solution. It is also my scientific opinion that, based on the cited references, one of skill in the art would have had no reasonable expectation of success in generating the claimed kits for measuring thrombin generation by combining the references.

Date: 10 Sept. 2007

By: _____
Peter Turecek, Ph.D.

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CURRICULUM VITAE

Name: Peter L. TURECEK, PhD

Adress: (business)
BAXTER AG
Industriestraße 67
A-1221 Vienna
+43-1-20100-2520
peter_turecek@baxter.com

Date of birth: May 9th, 1961
Place of birth: Vienna, Austria
Citizenship: Austria

Academic education:

1980 - 1985	Pharmacy, University of Vienna Degree: Magister pharmaciae 1985
1985 - 1987	Biochemistry, University of Vienna Thesis, Degree: Doctor rerum naturalium (Ph.D.) 1987
1980 - 1988	Business Administration, University of Economics, Vienna, Diploma 1988

Other training:

Protein chemistry, chromatography, process validation, hematology, coagulation, immunology

Specific fields of expertise:

Protein purification and characterization, plasma fractionation, virus inactivation, molecular biology, recombinant proteins, coagulation physiology, biochemical and analytical techniques, diagnostics, pharmaceutical biotechnology, pharmacology and toxicology

Professional experience:

present	Senior Director Preclinical R&D BioScience Division, Baxter Healthcare, BAXTER AG, Vienna
2001 - 2005	Director Global Preclinical R&D and Product Development BioScience Division, Baxter Healthcare, BAXTER AG, Vienna
2000 – 2001	Member Diagnostics Management Team, Research & Development Therapeutic Proteins Hyland Immuno Division, Baxter Healthcare, BAXTER AG, Vienna
1998 – date	Associate Professor of Pharmacology (Habilitation) University of Vienna
1997 - 1999	Head, Depts. Product & Process Development Coagulation and Pharmaceutical Technology, Global R&D Plasma, BAXTER/HYLAND-IMMUNO, Vienna
1996 - 1999	Head, Dept. of Process Monitoring Coagulation, Production Blood-Plasma Derivatives, Österreichisches Institut für Hämoderivate GesmbH, Vienna
1996 - date	Legal Permission for Animal Experiments (Tierversuchsleiter gem. Österr. Tierversuchsgesetz 1988)
1992 - 1995	Head, Dept. of Biochemical Research on Haemostasis and Thrombolysis, IMMUNO AG, Vienna

1991 - 1992	Deputy Head, Dept. of Biochemical Research on Coagulation and Fibrinolysis, IMMUNO AG, Vienna
1991	Head, Laboratory of Recombinant Blood Factors, Biomedical Research Center, IMMUNO AG, Orth
1989 - 1990	Research Assistant, Dept. of Microbiology and Molecular Biology, Biomedical Research Center, IMMUNO AG, Orth
1988 - 1989	Assistant Professor, Institute of Biochemistry, University of Vienna
1986 - 1989	Consultant for R&D Projects for MAGINDAG, Steirische Magnesit Industrie AG, Vienna and Research Biotechnology, Chemie Holding AG, Linz
1985 - 1988	Technician, Institute of Biochemistry, University of Vienna
1982	Laboratory Assistant, Dept. of Radiopharmaceuticals, Institute of Chemistry, Österreichisches Forschungszentrum, Seibersdorf
1980	Laboratory Assistant, Polymer Laboratory, Reichhold Chemie GmbH., Vienna

Technical and Scientific Expert in front of National and International Authorities (since 1992):

- European Patent-Office
- US Patent and Trademark Office
- German Patent-Office
- Austrian Patent-Office
- Paul-Ehrlich-Institute, Germany
- Medicines and Healthcare products Regulatory Agency (MHRA) – United Kingdom
- Agence française de sécurité sanitarie des produits de santé (AFSSAPS) – France
- Istituto Superiore di Sanità (ISS) – Italy
- Agenzia Italiana del Farmaco – Italy
- DIN Deutsches Institut für Normung e. V. NAMed AA C 5 - Arbeitsausschuss Hämatologie
- EDQM-European Pharmacopoeia Commission – Permanent Specialist Group of Experts Nr. 6B on Human Blood and Blood Products (since 2003)
- European Agency for the Evaluation of Medicinal Products (EMEA)
- US Department of Health and Human Services: Food and Drug Administration (FDA)
- European Commission, Directorate-General XII Science, Research and Development Group of Experts on Demonstration in Life Sciences (1998)

Teaching Experience:

- Lectureship at the University of Vienna in Pharmacology and Toxicology (since 1998):
- Lectures on Pharmaceutical Biotechnology,
- Lectures for Diploma and PhD-Students,
- Course on Pharmacology, Pharmacotherapy, Toxicology and Bromatology III (2002-2003)
- Lectureship Entrepreneurship MBA Applied Biomedicine, Donau-University Krems (2002)
- Lectureship Professional MBA Biotech Management, Donau-University Krems (2003)
- Lectureship in Pharmacology, FH-Studiengang „Medical and Pharmaceutical Biotechnology", University of Applied Management Sciences, Fachhochschule Krems (since 2003)
- Lectureship FH-Studiengang „Biotechnologie", FH-Campus Wien

(2003)

Honorary Positions and Memberships:

- Council, "Höhere Bundes-Lehr- und Versuchsanstalt für chemische Industrie", Vienna XVII, Rosensteingasse (1998 - 2002)
- Development Team FH-Studiengang Medical and Pharmaceutical Biotechnology, International Management Center, Fachhochschule Krems (2001-2002)
- „Wirtschaftsboard", University of Applied Management Sciences, Fachhochschule Krems (since 2003)
- Austrian Biochemical Society
- Austrian Society of Biotechnology
- Austrian Pharmaceutical Society
- World Federation of Haemophilia
- The Protein Society
- The International Society on Thrombosis and Haemostasis

Ad hoc Reviewer:

- Biotechnology Journal
- Blood
- Blood Coagulation Fibrinolysis
- Journal of Thrombosis and Haemostasis
- Thrombosis and Haemostasis
- Thrombosis Research

Grants and Awards:

- Research Grant "Jubiläumsfonds der Österr. Nationalbank" (1987-1988)
- 12 Baxter Technical Awards 1998 (Categories: Distinguished Corporate Contribution, Special Accomplishment)
- 7 Baxter Technical Awards 1999 (Categories: Customer First, Special Accomplishment)
- 6 Baxter Technical Awards 2000 (Categories: Customer First, Special Accomplishment, Outstanding Corporate Achievement)
- Baxter Technical Award 2003 (Category: Outstanding Innovation)
- Baxter Technical Award 2005 (Category: Distinguished Contribution)

Number of Publications: 93 papers and book articles
225 lectures and abstracts

Number of Granted, Published or Filed Patents: 412 (46 patent families)

EXHIBIT B

1

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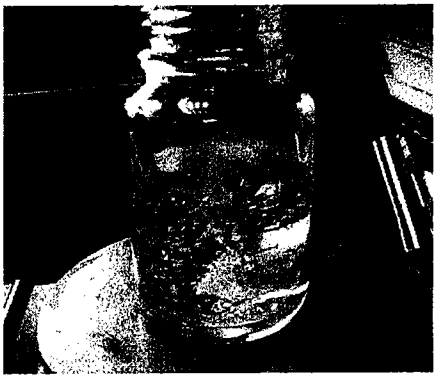

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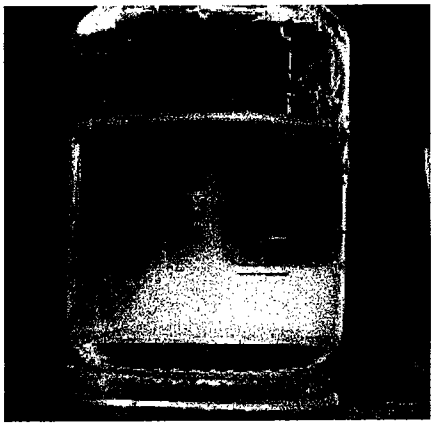

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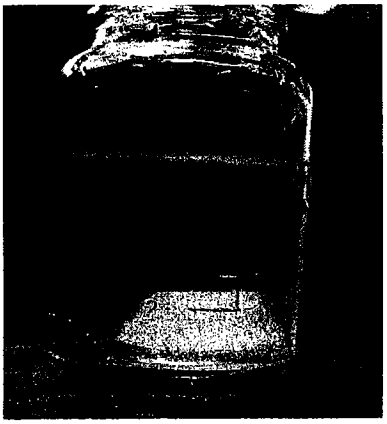

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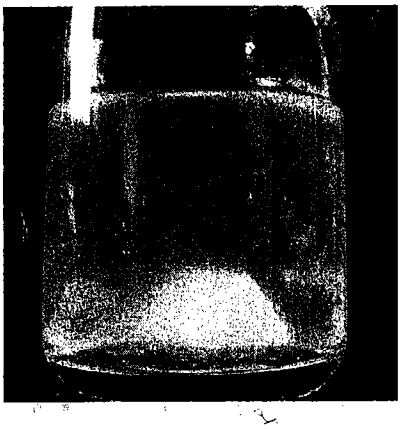

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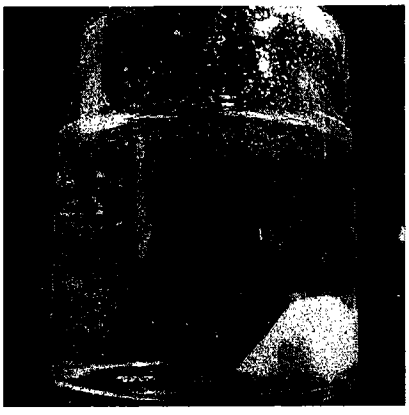

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